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 DOCUMENT NUMBER: 122:32021  
 TITLE: Process for preparing cyclosporin A derivatives  
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OTHER SOURCE(S):	CASREACT 122:32021			
GI				

Q-?-Abu-Sar-MeLeu-Val-MeLeu-Ala-D-Ala-MeLeu-MeLeu-MeVal

I

AB A process for prepg. cyclosporin A derivs., namely I [Q = (2S,3R,4R)-3-hydroxy-4,7-dimethyl-2-methylamino-8-oxooctanoic acid (A) or the isomeric (2S,3R,4R)-3-hydroxy-4-methyl-2-methylamino-9-oxononanoic acid (B)], is disclosed. The process involves hydroformylation of an organic (especially PhMe) solution of cyclosporin A (II) by a mixture of CO and H<sub>2</sub> (preferably 1:1 mol ratio) at 25-200° and 0.1-30 MPa, for 10 min to 4 h, in the presence of a Co- or Rh-based catalyst. I are useful as immunosuppressants (no data). The aldehyde group in I also allows binding to a macromol. carrier without loss of biol. activity, allowing antibodies to II and proteins binding to II to be obtained (no data). For example, II was autoclaved with Rh<sub>4</sub>(CO)<sub>12</sub> in benzene under 5.5 MPa 1:1 (volume) CO/H<sub>2</sub> gas mixture at 60° for 60 min to give I (Q = A, both R and S epimers at C-7) with 70% conversion and 60% selectivity. Use of Rh(acac)(CO)<sub>2</sub> (acac = acetylacetonate) as catalyst also gave I (Q = A), with 88% conversion and 63% selectivity, whereas Co(CO)<sub>8</sub> gave I (Q = B) with 82% conversion and 80% selectivity.

IT 59865-13-3DP, Cyclosporin A, aldehydic derivs.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of cyclosporin A derivs. by hydroformylation)

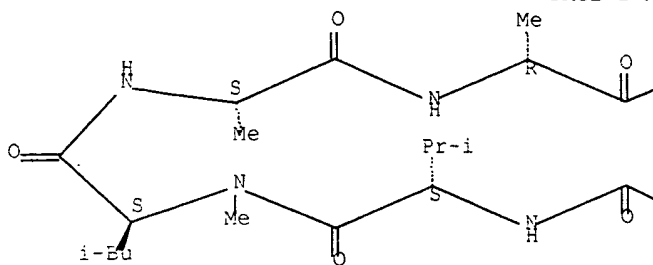
RN 59865-13-3 HCAPLUS

CN Cyclosporin A (9CI) (CA INDEX NAME)

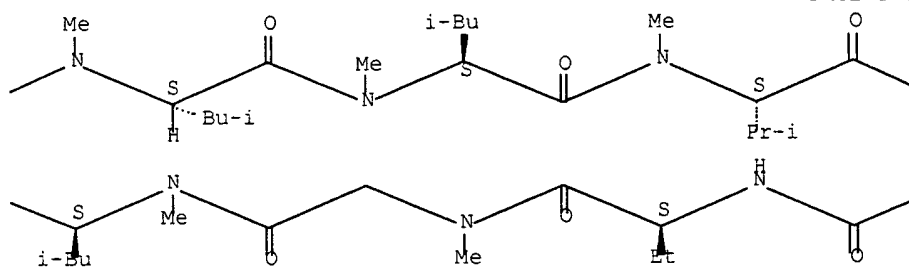
Absolute stereochemistry.

Double bond geometry as shown.

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PAGE 1-B



PAGE 1-C

